Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 619–630

TETRAHEDRON

A simple synthetic approach to homochiral 6- and 6′-substituted 1,1′-binaphthyl derivatives

Heiko Hocke and Yasuhiro Uozumi*

Institute for Molecular Science (IMS), Nishi-Gonaka 38, Myodaiji, Okazaki 444-8585, Japan

Received 9 October 2002; accepted 2 December 2002

Abstract—Various homochiral binaphthyl derivatives having functional groups at the 6-position are important key intermediates for the immobilization of binaphthyl compounds on various solid-supports and have been prepared from commercially available 1,1′-bi-2-naphthol via controlled monopivalation of the 2-hydroxyl group and electrophilic aromatic substitution at the 6-position. (*S*)-2,2′-Bis-((*S*)-4-alkyloxazol-2-yl)-6-(2-methoxycarbonyl)ethyl-1,1′-binaphthyls (6-functionalized (*S*,*S*)-boxax)) were prepared and immobilized on various polymer supports including PS–PEG, PS, PEGA and MeO–PEG resin.

1. Introduction

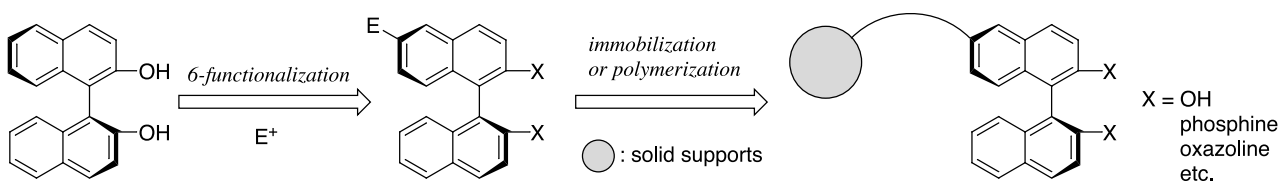
Enantiomerically pure 1,1′-binaphthyl derivatives have been found to be highly useful as basic chiral units in various fields of chemistry. In particular, the C_2-symmetric 2,2′-difunctionalized-1,1′-binaphthyls (e.g. 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl (BINAP), 2,2′-dihydroxy-1,1′-binaphthyl (BINOL), etc.) are recognized as one of the most powerful classes of chiral ligands in asymmetric catalyses.[1]

Immobilization of homogeneous catalysts has been attracting significant interest because it could combine the advantages of both homogeneous and heterogeneous catalysts in one system.[2] Recently, many research groups have been investigating ways to immobilize chiral binaphthyl-based catalysts on solid supports where the attachment has been achieved usually at the 6-position of the binaphthyl backbone (Scheme 1).[3] However, since the 6- and 6′-positions of bi-2-naphthol are equally activated toward electrophilic aromatic substitution by the 2,2′-hydroxyl groups, the methods reported thus far for introducing 6-substituents have resulted in producing a nearly statistical ratio of non-/mono-/bis-substituted products to require costly chromatographic separation.[4] There is good reason to believe that development of a flexible and efficient route to diversely substituted enantiomerically pure binaphthyl compounds bearing various functional groups at their 6-position would offer a practical method for the immobilization of chiral binaphthyl-based catalysts. In this paper, we report a simple synthetic approach to enantiomerically pure 6-substituted-1,1′-binaphthyl derivatives via monofunctionalization at the 6-position of the binaphthyl skeleton starting from commercially available (*S*)-1,1′-bi-2-naphthol (**1**). Immobilization of 2,2′-bis(oxazol-2-yl)-1,1′-binaphthyls, the so-called boxax, on various polymer supports including PS–PEG, PS, PEGA and MeO–PEG resin was achieved via (*S*)-2,2′-bis((*S*)-4-alkyloxazol-2-yl)-1,1′-binaphthyls prepared by the presented method.[5]

2. Results and discussion

2.1. Monofunctionalization of the 6-position

Bi-2-naphthol **1** is a C_2-symmetric axially chiral aromatic

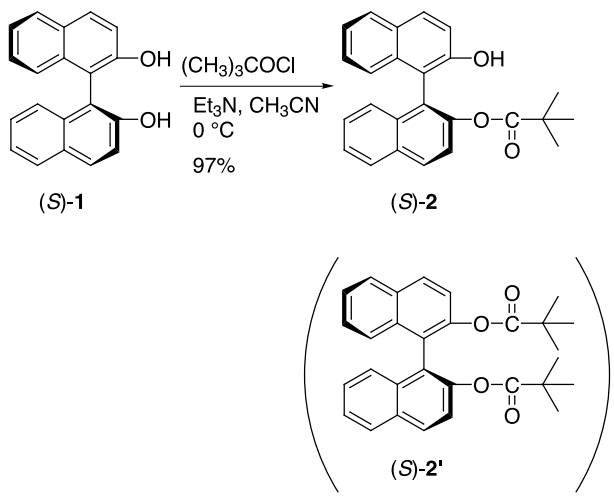


Scheme 1.

Keywords: 1,1′-binaphthyls; immobilization; polymer-supports.

* Corresponding author. Tel./fax: +81-564-55-7240; e-mail: uo@ims.ac.jp

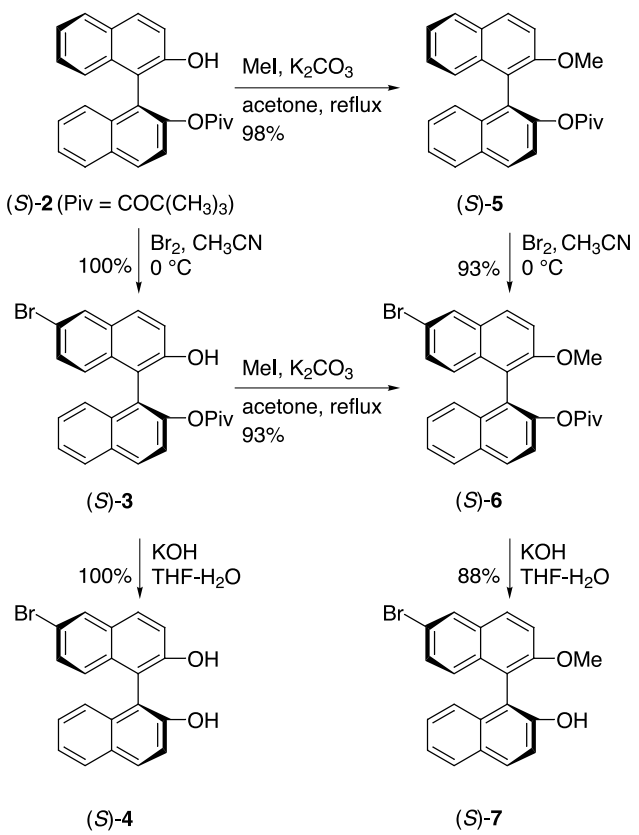
0040–4020/03/$ - see front matter
PII: S0040-4020(02)01584-3



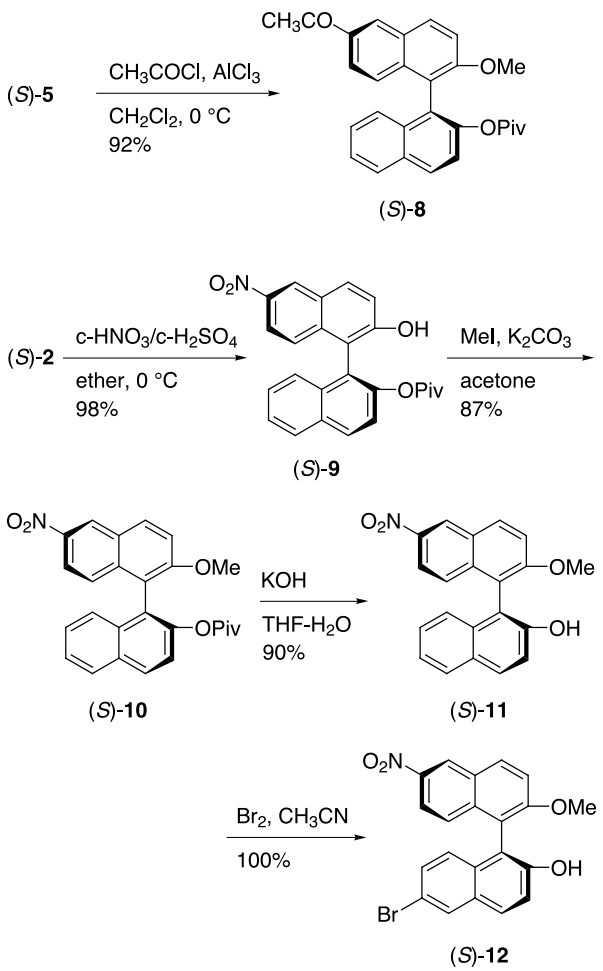
Scheme 2.

molecule in which the 6- and 6′-positions are equally activated toward electrophilic aromatic substitution by the 2,2′-hydroxyl groups. By introducing an appropriate substituent at one of the 2-positions, the electronic character of the naphthalene units are altered making the 6- and 6′-positions distinguishable, one from the other. The controlled monoesterification of the 2,2′-dihydroxyl groups with a bulky pivaloyl group was found to be suitable for this purpose.[6] Thus, the reaction of (*S*)-binaphthol ((*S*)-**1**) and pivaloyl chloride in the presence of triethylamine in acetonitrile at 0°C gave (*S*)-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-**2**) as a single product in 97% yield (Scheme 2). Due to the steric bulkiness of the resulting 2′-pivalate group of **2**, subsequent esterification of the 2-hydroxyl group forming the dipivalate **2′** was almost completely suppressed.

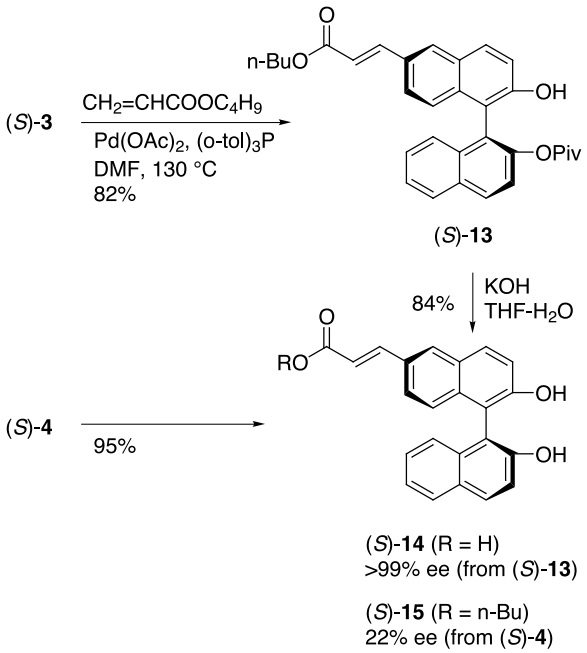
Electrophilic monosubstitution at the 6-position of the pivalate **2** was first examined for bromination where the 6′-position should be deactivated by the electron withdrawing character of the pivalate group at the 2′-position (Scheme 3). Compound (*S*)-**2** was treated with 2 equiv. of bromine in acetonitrile at 0°C for 2 h. After quenching with aqueous Na_2SO_3, the analytically pure (*S*)-6-bromo-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-**3**) was obtained by simple extraction in quantitative yield without further chromatographic purification or recrystallization. Detailed ^1H and ^{13}C NMR analysis revealed that neither the 6,6′-dibrominated product nor any regioisomeric products were formed. The pivaloyl group was readily cleaved by saponification with potassium hydroxide in a mixture of THF/H_2O at 25°C for 14 h, and the resulting (*S*)-6-bromo-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-**4**) was isolated by simple extraction in quantitative yield. The enantiomeric purity of binaphthol (*S*)-**4** was determined by HPLC to be over 99% ee. It should be noted that no costly chromatography was required throughout these two steps and that the synthetic sequence was performed in our laboratory on a 20 g scale. (*S*)-2-Methoxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-**5**), which was readily prepared from (*S*)-**2** by methylation with



Scheme 3.



Scheme 4.



Scheme 5.

MeI/K_2CO_3, underwent controlled monobromination successfully under conditions similar to those described for (*S*)-**3** to give (*S*)-6-bromo-2-methoxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-**6**) in 93% yield. Methylation of (*S*)-**3** also gave (*S*)-**6** in 93% yield. Alkaline hydrolysis of the pivaloyl group of (*S*)-**6** gave (*S*)-**7** where functionalization of the 2 and 6-positions of the starting binaphthol (**2**) was achieved.

The utility of 2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-**2**) as a key intermediate for selective monofunctionalization of the 6-position has been examined for Friedel–Crafts acylation and nitration (Scheme 4). Thus, 2-methoxy-2′-pivaloyloxybinaphthyl (*S*)-**5** was treated with acetyl chloride and $AlCl_3$ in dichloromethane at 0°C to give the 6-acetylated (*S*)-**8** as a single product in 92% yield. Analytically pure (*S*)-**8** was obtained by simple extraction after aqueous workup (Scheme 4). Nitration of the pivalate (*S*)-**2** proceeded smoothly under two-phase conditions using ether with a mixture of HNO_3/H_2SO_4 at 0°C. Workup by simple extraction gave (*S*)-6-nitro-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-**9**) in 98% yield. Here again, no chromatographic purification was required to isolate the analytically pure nitrobinaphthyl (*S*)-**9**. Methylation of the nitro ester (*S*)-**9** using MeI/K_2CO_3 followed by deprotection of the pivaloyl group under aqueous alkaline conditions gave compound (*S*)-**11**. Bromination of (*S*)-**11** with bromine as described for (*S*)-**3** gave (*S*)-6′-bromo-6-nitro-2′-hydroxy-2-methoxy-1,1′-binaphthyl ((*S*)-**12**) carrying four different functional groups at the 2,2′,6 and 6′-positions in an overall yield of 74% (starting from binaphthol (*S*)-**1**, 5 steps). It should be pointed out that each substituent of (*S*)-**12** can be subjected to further transformations independently. The bromide (*S*)-**3** was also successfully applied to the Heck reaction (Scheme 5). The reaction of (*S*)-**3** with *n*-butyl acrylate proceeded smoothly at 130°C to give the desired Heck product (*S*)-**13** in 82% yield. Thorough investigations have shown that tri-*n*-butylamine as base and $Pd(OAc)_2/(o\text{-tol})_3P$ as catalyst are essential for a high yield of (*S*)-**13**. Saponification of the ester groups with potassium hydroxide gave the acid (*S*)-**14** in 84% yield. Exclusive formation of the *trans*-Heck product **14** was confirmed by the coupling constant (15.9 Hz) of the olefinic protons[7] in the ^1H NMR spectrum. The enantiomeric purity of (*S*)-**14** was determined to be >98% indicating that even at high reaction temperatures and for long reaction times the steric bulkiness of the pivaloyl group prevents racemization at the chiral axis while under similar reaction conditions the bromobinaphthol (*S*)-**4** suffered partial racemization giving 22% ee of (*S*)-**15**.

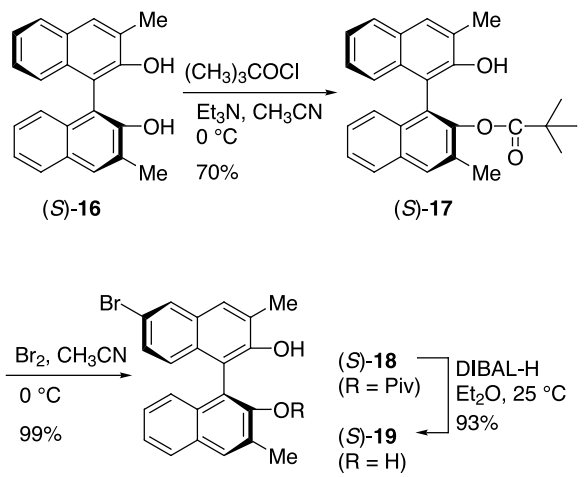
2.2. Functionalization of 3,3′-disubstituted 2,2′-dihydroxy-1,1′-binaphthyls

The monopivalate-based approach for the selective monosubstitution at the 6-position of binaphthyls was also successfully applied for the preparation of (*S*)-6-bromo-3,3′-dimethyl-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-**19**) (Scheme 6). Thus, the bromide (*S*)-**18** was obtained via the pivalate (*S*)-**17** which was readily prepared by the pivalation of 3,3′-dimethyl-binaphthol (*S*)-**16**.[8] Bromination of the pivalate (*S*)-**17** in acetonitrile at 0°C for 1 h gave 99% of the monobromide (*S*)-**18** as the single product. The pivaloyl group was cleaved by reduction with DIBAL-H or alkaline hydrolysis to give (*S*)-**19**[9] in high yield, the overall yield from (*S*)-**16** being 65% (3 steps, Scheme 6).

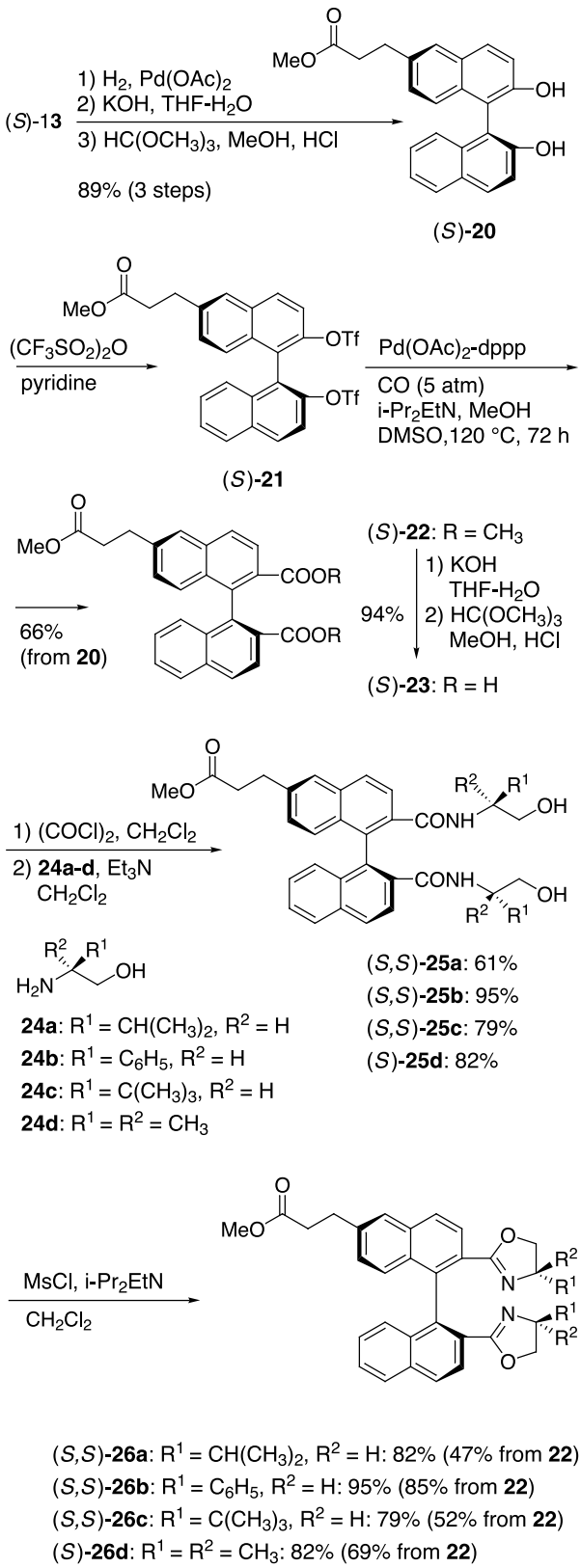
2.3. Polymer-supported boxax ligands

Immobilization of the binaphthyl-based chiral ligands was examined for that of 2,2′-bis(oxazol-2-yl)-1,1′-binaphthyls. Recently, we have developed optically active bis(oxazoline) ligands 2,2′-bis(oxazol-2-yl)-1,1′-binaphthyls (boxax), which are useful as chiral ligands for copper(I)-catalyzed cyclopropanations[10] and palladium(II)-catalyzed Wacker-type cyclizations.[11] Thus, for example, a palladium(II) complex of (*S*)-2,2′-bis((*S*)-4-isopropyloxazol-2-yl)-1,1′-binaphthyl ((*S*,*S*)-ip-boxax) catalyzed cyclization of 2-(2,3-dimethyl-2-butenyl)phenol to give (*S*)-2-methyl-2-isopropenyl-2,3-dihydrobenzofuran with up to 98% ee.

Boxax ligands bearing carboxylic tether groups at their



Scheme 6.



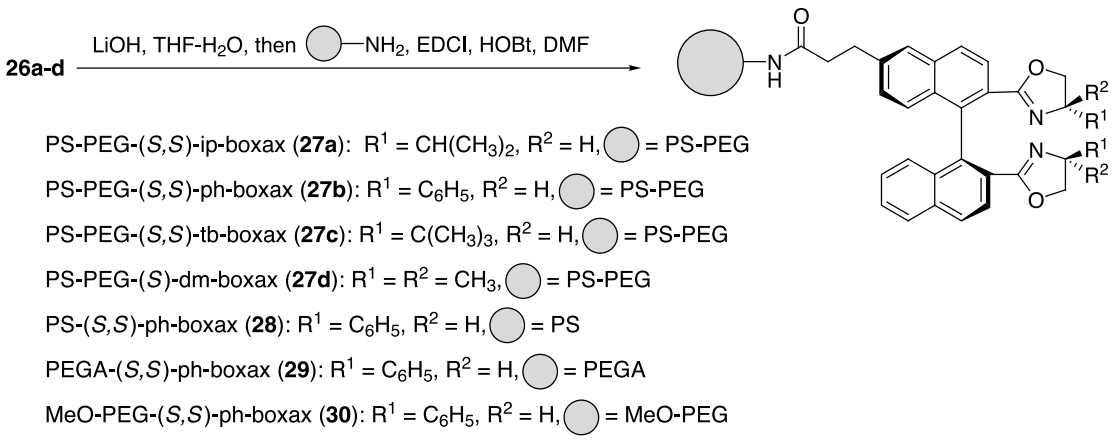
Scheme 7.

6-positions were prepared from the Heck product (*S*)-**13** (Scheme 7) and were anchored on various polymer supports (Scheme 8). Thus, the Heck product (*S*)-**13** was converted to 2,2′-dihydroxy-6-(2-methoxycarbonyl)ethyl-1,1′-binaphthyl (**20**) in 89% yield (3 steps) via hydrogenation of the olefin, saponification of the ester groups, and methyl esterification of the resulting carboxylic acid. Introduction of oxazolinyl groups at both the 2- and 2′-positions was performed according to our reported procedure for the preparation of various boxax ligands. Thus, after treatment of **20** with triflic anhydride, the resulting triflate **21** was subjected to palladium-catalyzed carbonylation in the presence of $Pd(OAc)_2$/dppp catalyst and diisopropylethylamine in DMSO–MeOH at 120°C for 72 h under 5 atm of carbon monoxide to afford (*S*)-2,2′-bis(methoxycarbonyl)-6-(2-methoxycarbonyl)ethyl-1,1′-binaphthyl ((*S*)-**22**) in 66% yield.[12] The triester **22** was hydrolyzed under aqueous alkaline conditions and the resulting 6-aliphatic acid was selectively protected to give 2,2′-bis(hydroxycarbonyl)-1,1′-binaphthyl (*S*)-**23**. Condensation of the diacid **23** with aminoalcohols, (*S*)-valinol (**24a**), (*S*)-phenylglycinol (**24b**), (*S*)-*t*-leucinol (**24c**) and 2-amino-2-methyl-1-propanol (**24d**), via the binaphthylcarboxylic dichloride which was generated by treatment of **23** with oxalyl chloride, gave the 2,2′-bis(carboamides) **25a–d**. The oxazoline ring formation was performed by treatment of **25a–d** with methanesulfonyl chloride in the presence of diisopropylethylamine to give 6-(2-methoxycarbonyl)ethyl-2,2′-bis(oxazol-2-yl)-1,1′-binaphthyl (*S*,*S*)-**26a**, (*S*,*S*)-**26b**, (*S*,*S*)-**26c** and (*S*)-**26d** in 47, 85, 79 and 69% yields (from **22**, 5 steps), respectively.

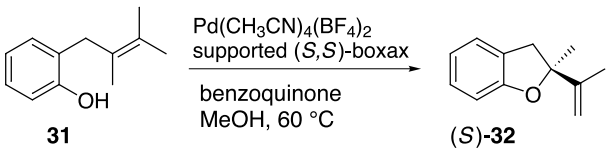
The immobilization of the 6-functionalized boxax ligands **26** thus prepared was examined on various polymer supports including polystyrene–poly(ethylene glycol) (PS–PEG),[13] polystyrene (PS),[14] a copolymer of acrylamidopropyl[2-aminopropyl]poly(ethylene glycol) and *N*,*N*-dimethylacrylamide (PEGA),[15] and methoxy poly(ethylene glycol) (MeO–PEG)[16,17] bearing terminal amino groups. Thus, for example, alkaline hydrolysis of the carboxy esters of **26a** with lithium hydroxide in aqueous THF gave the corresponding lithium carboxylate quantitatively, leaving the oxazoline groups intact. A mixture of the resulting carboxylate and PS–PEG amino resin was shaken at 25°C under the standard conditions for solid-phase amide condensation using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI) and 1-hydroxybenzotriazole hydrate (HOBt) in DMF to give a quantitative yield of PS–PEG resin-supported (*S*,*S*)-ip-boxax ligand **27a** (Scheme 8). The boxax ligands **27b–d** having phenyl, *t*-butyl and dimethyl substituents on their oxazoline rings were attached to PS–PEG amino resin under the same reaction conditions to give PS–PEG-(*S*,*S*)-ph-boxax (**27b**), PS–PEG-(*S*,*S*)-tb-boxax (**27c**) and PS–PEG-(*S*)-dm-boxax (**27d**), respectively. PS-, PEGA- and MeO–PEG-supported ph-boxax **28**, **29** and **30** were also prepared under similar conditions.

2.4. Asymmetric Wacker-type cyclization with polymer-supported boxax ligands[5]

The enantiocontrolling ability of polymer-supported boxax ligands was examined for Wacker-type cyclization of 2-(2,3-dimethyl-2-butenyl)phenol (**31**) forming optically active 2-methyl-2-isopropenyl-2,3-dihydrobenzofuran (**32**) (Scheme 9). A mixture of the supported complexes generated by mixing the polymer-supported boxax ligands above prepared with $Pd(CH_3CN)_4{\cdot}(BF_4)_2$ and the allylphenol **31** was shaken at 60°C for 20 h in methanol in the



Scheme 8.



boxax	yield	% ee
27b	10%	91% ee
28	14%	84% ee
30	46%	96% ee

Scheme 9.

presence of 4 equiv. of benzoquinone to give the benzofuran **32** the enantiomeric purity and absolute configuration of which were determined by GC analysis with chiral stationary phase capillary column (cyclodex β236M19). The representative results are shown in Scheme 9. It was found that the stereoselectivity provided by amphiphilic PS–PEG and MeO–PEG polymer-supported boxax ligands **30** reached a comparable level to that observed in the solution-phase using (*S*,*S*)-boxax ligands,[11] though the catalytic activity of the supported complexes was much lower than that of the corresponding homogeneous catalysts. Thus, for example, the Wacker-type cyclization of **31** with a palladium(II) complex of MeO–PEG-(*S*,*S*)-ph-boxax **30** gave the benzofuran **32** in 46% isolated yield with 98% reaction selectivity and 95% stereoselectivity.

3. Conclusion

In conclusion, we have developed a simple method for the preparation of asymmetric optically pure 2,2′,6,6′-tetra-substituted binaphthyl derivatives starting from the commercially available 1,1′-bi-2-naphthol (**1**). This method is highly flexible and allows the design of a broad variety of highly functionalized binaphthyl derivatives including 3,3′-substituted alkyl derivatives. Asymmetric functionalization of the 6- and/ or 6′-positions would also allow fine-tuning of the electronic character of the 2- and 2′-functional groups of binaphthyls which have recently found utility in several asymmetric catalytic processes.[18]

4. Experimental

4.1. General

All manipulations were carried out under a nitrogen atmosphere. Nitrogen gas was dried by passage through P_2O_5 (Merck, SICAPENT). NMR spectra were recorded on a JEOL JNM-AL400 spectrometer (400 MHz for ^{1}H NMR), or JEOL JNM LA500 spectrometer (500 MHz for ^{1}H and 125 MHz for ^{13}C). Chemical shifts are reported in δ ppm referenced to an internal $SiMe_4$. NMR spectra were recorded in $CDCl_3$ at 25°C if not mentioned otherwise. Optical rotations were measured on a JASCO DIP-370 polarimeter.

4.1.1. (*S*)-2-Hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-2). To a solution of (*S*)-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-**1**) (5.726 g, 20.0 mmol) and triethylamine (8.4 mL, 60.0 mmol) in acetonitrile (60 mL) was added pivaloyl chloride (2.435 g, 20.2 mmol) dropwise over a period of 1 h at 0°C. The mixture was allowed to warm to 25°C and stirred for 4 h. The reaction mixture was diluted with ether (150 mL) and washed with aqueous 1N HCl (30 mL, 2 times), saturated aqueous $NaHCO_3$ (30 mL, 2 times), and brine (30 mL, 2 times). The organic phase was dried over $MgSO_4$ and the solvent was evaporated. The residue was purified by column chromatography over silica gel with *n*-hexane/EtOAc (6:1) to give (*S*)-**2** (7.16 g, 97%) as white solid: $[\alpha]_D^{25}=-56.8$ (*c* 0.51, THF); ^{1}H NMR δ 0.78 (s, 9H), 5.13 (s, 1H), 7.06 (d, *J*=8.4 Hz, 1H), 7.23–7.39 (m, 6H), 7.51 (t, *J*=5.8 Hz, 1H), 7.82 (d, *J*=7.6 Hz, 1H), 7.88 (d, *J*=8.8 Hz, 1H), 7.98 (d, *J*=8.0 Hz, 1H), 8.08 (d, *J*=8.8 Hz, 1H); ^{13}C NMR δ 26.51, 38.79, 114.18, 118.16, 121.74, 122.91, 123.43, 124.49, 125.54, 126.12, 126.56, 127.36, 127.81, 128.23, 128.94, 130.18, 130.62, 132.11, 133.40, 133.53, 148.22, 151.65, 177.67. Anal. calcd for $C_{25}H_{22}O_3$: C, 81.06; H, 5.99. Found: C, 80.88; H, 6.11.

4.1.2. (*S*)-6-Bromo-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-3). To a solution of (*S*)-**2** (7.10 g, 19.2 mmol) in acetonitrile (100 mL) was slowly added bromine (1.96 mL, 38.3 mmol) at 0°C. The reaction mixture was stirred at 0°C for 2 h and quenched with aqueous Na_2SO_3. After addition of 200 mL of ether, the organic phase was washed with saturated aqueous $NaHCO_3$,

aqueous 1N HCl and brine, and dried over $MgSO_4$. After removal of the solvent, (*S*)-**3** (8.86 g, 100%) was obtained as a white solid: $[\alpha]_D^{25}=+6.22$ (*c* 0.52, THF); ^{1}H NMR δ 0.81 (s, 9H), 5.18 (s, 1H), 6.92 (d, *J*=8.8 Hz, 1H), 7.25–7.40 (m, 5H), 7.51 (td, J_1=7.2 Hz, J_2=1.2 Hz, 1H), 7.79 (d, *J*=8.8 Hz, 1H), 7.98 (m, 2H), 8.08 (d, *J*=8.8 Hz, 1H); ^{13}C NMR δ 26.63, 38.87, 114.42, 117.19, 119.29, 121.68, 122.18, 125.23, 126.18, 126.30, 127.45, 128.26, 129.19, 129.72, 129.75, 129.96, 130.86, 132.04, 133.19, 148.13, 151.95, 177.52. Anal. calcd for $C_{25}H_{21}O_3Br$: C, 66.83; H, 4.71. Found: C, 66.95; H, 4.88.

4.1.3. (*S*)-6-Bromo-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-4). *Method A*. A mixture of (*S*)-**3** (6.74 g, 15.0 mmol), potassium hydroxide (2.52 g, 45.0 mmol), THF (60 mL), and water (20 mL) was stirred for 14 h at 25°C under nitrogen. The reaction mixture was diluted with EtOAc (150 mL) and the organic phase was washed with aqueous 1N HCl (50 mL), saturated aqueous $NaHCO_3$ (30 mL, 5 times), and brine (30 mL, 2 times). The organic phase was dried over $MgSO_4$ and concentrated in vacuo to give (*S*)-**4** (5.50 g, 100%) as a yellow solid: $[\alpha]_D^{25}=+6.3$ (*c* 0.49, THF); ^{1}H NMR δ 4.99 (s, 1H), 5.08 (s, 1H), 7.02 (d, *J*=8.0 Hz, 1H), 7.09 (d, *J*=7.2 Hz, 1H), 7.30–7.41 (m, 5H), 7.51 (t, *J*=5.8 Hz, 1H), 7.87–7.90 (m, 2H), 7.98 (d, *J*=8.6 Hz, 1H), 8.04 (s, 1H); ^{13}C NMR δ 110.18, 111.25, 117.78, 117.86, 118.93, 123.99, 124.19, 126.11, 127.66, 128.49, 129.47, 130.36, 130.44, 130.58, 130.69, 131.70, 132.01, 133.27, 152.72, 153.00. Anal. calcd for $C_{20}H_{13}O_2Br$: C, 65.77; H, 3.59. Found: C, 65.56; H, 3.80. The enantiomeric purity of **4** was determined by HPLC analysis with a chiral stationary phase column to be >99% ee (Daicel OD-H, *n*-hexane/isopropanol 10:1, flow 0.5 mL/min, (*S*)-**4** 36.6 min, (*R*)-**4** 53.1 min).

4.1.4. (*S*)-2-Methoxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-5).[19] A mixture of (*S*)-**2** (3.70 g, 10.0 mmol), methyl iodide (2.83 g, 1.24 mL, 20.0 mmol), potassium carbonate (2.70 g, 20.0 mmol) and acetone (40 mL) was refluxed for 16 h. After being cooled to ambient temperature, the mixture was concentrated in vacuo and the residue was poured into a separatory funnel with EtOAc and water. After phase separation, the organic phase was washed with aqueous sodium thiosulfate (3%, 30 mL), water, and brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography over silica gel with *n*-hexane/EtOAc (4:1) affording (*S*)-**5** (3.77 g, 98%) as a white powder: $[\alpha]_D^{25}=-41.8$ (*c* 0.52, THF); ^{1}H NMR δ 0.71 (s, 9H), 3.74 (s, 3H), 7.12 (d, *J*=8.8 Hz, 1H), 7.22 (t, *J*=7.2 Hz, 1H), 7.27–7.31 (m, 3H), 7.39–7.45 (m, 3H), 7.82 (d, *J*=8.0 Hz, 1H), 7.92 (d, *J*=8.0 Hz, 1H), 7.94 (d, *J*=8.8 Hz, 1H), 7.97 (d, *J*=8.8 Hz, 1H); ^{13}C NMR δ 26.53, 38.64, 56.80, 113.68, 117.99, 121.93, 123.57, 125.13, 125.27, 125.32, 125.98, 126.27, 126.43, 127.54, 128.02, 128.80, 128.95, 129.73, 131.63, 133.67, 133.76, 146.85, 154.90, 176.15. Anal. calcd for $C_{26}H_{24}O_3$: C, 81.26; H, 6.24. Found: C, 80.81; H, 6.17.

4.1.5. (*S*)-6-Bromo-2-methoxy-2′pivaloyloxy-1,1′-binaphthyl ((*S*)-6). *From* (*S*)-**3**. A mixture of (*S*)-**3** (3.06 g, 6.81 mmol), methyl iodide (1.93 g, 0.848 mL, 13.63 mmol), potassium carbonate (1.84 g, 13.63 mmol) and acetone (40 mL) was refluxed for 16 h. Acetone was removed in vacuo, water was added to the residue and the mixture was extracted with CH_2Cl_2 (60 mL, 3 times). The organic phase was dried over $MgSO_4$. After removal of the solvent in vacuo, the resulting residue was purified by column chromatography over silica gel with *n*-hexane/EtOAc (5:1) to give (*S*)-**6** (2.94 g, 93%) as a white solid.

From (*S*)-**5**. To a solution of (*S*)-**5** (768 mg, 2.0 mmol) in acetonitrile (20 mL) was added bromine (0.2 mL, 4.0 mmol). The mixture was stirred for 2 h at 0°C and quenched with aqueous Na_2SO_3. After addition of 50 mL of EtOAc, the organic phase was washed with saturated aqueous $NaHCO_3$, aqueous 1N HCl and brine and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography over silica gel with *n*-hexane/EtOAc (2:1) to give (*S*)-**6** (861 mg, 93%): $[\alpha]_D^{25}=+14.2$ (*c* 0.54, THF); ^{1}H NMR δ 0.75 (s, 9H), 3.75 (s, 3H), 7.00 (d, *J*=9.0 Hz, 1H), 7.22 (d, *J*=8.3 Hz, 1H), 7.26–7.31 (m, 2H), 7.39 (d, *J*=9.0 Hz, 1H), 7.42 (d, *J*=9.0 Hz, 1H), 7.45 (t, *J*=7.6 Hz, 1H), 7.86 (d, *J*=9.0 Hz, 1H), 7.94 (d, *J*=8.3 Hz, 1H), 7.97–7.99 (m, 2H); ^{13}C NMR δ 26.76, 38.86, 56.94, 114.81, 117.69, 118.46, 122.21, 124.77, 125.72, 126.02, 126.79, 127.55, 128.45, 129.17, 129.46, 129.80, 130.05, 130.20, 131.96, 132.59, 133.80, 147.23, 155.51, 176.58. Anal. calcd for $C_{26}H_{23}O_3Br$: C, 67.39; H, 5.00. Found: C, 67.21; H, 4.98.

4.1.6. (*S*)-6-Bromo-2-methoxy-2′-hydroxy-1,1′-binaphthyl ((*S*)-7). A mixture of (*S*)-**6** (1.389 g, 3.0 mmol), potassium hydroxide (0.513 g, 9.0 mmol), THF (15 mL) and water (10 mL) was stirred at 60°C for 16 h. The reaction mixture was diluted with EtOAc (100 mL) and washed with saturated aqueous $NaHCO_3$, water and brine. After being dried over $MgSO_4$, the mixture was concentrated in vacuo. The residue was purified by column chromatography over silica gel using *n*-hexane/EtOAc (3:1) to afford (*S*)-**7** (998 mg, 88%) as a white solid: $[\alpha]_D^{25}=-7.73$ (*c* 0.67, THF); ^{1}H NMR δ 3.80 (s, 3H), 4.86 (s, 1H), 6.98 (dd, J_1=8.4 Hz, J_2=0.8 Hz, 1H), 7.03 (d, *J*=8.8 Hz, 1H), 7.22 (td, J_1=7.2 Hz, J_2=1.6 Hz, 1H), 7.25–7.35 (m, 3H), 7.49 (d, *J*=8.8 Hz, 1H), 7.85 (d, *J*=8.0 Hz, 1H), 7.90 (d, *J*=8.8 Hz, 1H), 7.95 (d, *J*=8.8 Hz, 1H), 8.05 (d, *J*=1.6 Hz, 1H); ^{13}C NMR δ 56.69, 114.32, 114.71, 115.69, 117.45, 117.94, 123.29, 124.51, 126.50, 126.77, 128.12, 129.05, 129.96, 130.00, 130.37, 130.49, 132.52, 133.52, 151.14, 156.03. Anal. calcd for $C_{21}H_{15}O_2Br$: C, 66.51; H, 3.99. Found: C, 66.61; H, 4.12.

4.1.7. (*S*)-6-Acetyl-2-methoxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-8). A mixture of (*S*)-**5** (384 mg, 1.0 mmol), anhydrous aluminum chloride (400 mg, 3.0 mmol) and CH_2Cl_2 (10 mL) was stirred at 0°C for 5 min. To the mixture was added acetyl chloride (157 mg, 2.0 mmol) and the reaction mixture was stirred for 3 h at 0°C. The reaction mixture was quenched with aqueous 1N HCl (50 mL) and extracted with CH_2Cl_2. The extract was dried over $MgSO_4$ and concentrated in vacuo to give a white powder. The powder was rinsed with *n*-hexane/EtOAc (5:1) affording (*S*)-**8** (393 mg, 92%) as a white powder: $[\alpha]_D^{25}=+36.6$ (*c* 0.51, THF); ^{1}H NMR δ 0.73 (s, 9H), 2.67 (s, 3H), 3.80 (s, 3H), 7.17 (d, *J*=8.8 Hz, 1H), 7.22 (d, *J*=8.0 Hz, 1H), 7.29 (td, J_1=6.8 Hz, J_2=1.2 Hz, 1H), 7.40 (d, *J*=8.8 Hz, 1H), 7.44–7.48 (m, 2H), 7.76 (dd, J_1=9.0 Hz,

J_2=1.7 Hz, 1H), 7.95 (d, J=8.2 Hz, 1H), 8.00 (d, J=9.0 Hz, 1H), 8.10 (d, J=9.0 Hz, 1H), 8.49 (d, J=1.8 Hz, 1H); ^{13}C NMR δ 26.54, 26.66, 38.63, 56.52, 113.97, 117.94, 121.87, 124.33, 124.66, 125.39, 125.61, 126.46, 127.65, 128.15, 129.18, 130.00, 131.63, 131.74, 132.37, 133.40, 136.13, 146.89, 157.00, 176.09, 197.69. Anal. calcd for $C_{28}H_{26}O_4$: C, 78.89; H, 6.10. Found: C, 79.01; H, 6.14.

4.1.8. (*S*)-6-Nitro-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-9). Pivalate (*S*)-**2** (2.81 g, 7.59 mmol) was added to a mixture of conc. nitric acid (5 mL), ether (60 mL) and conc. sulfuric acid (2 mL) at 0°C. The color of the reaction mixture turned yellow. After stirring for 2 h at 0°C, the mixture was poured into a mixture of ether (30 mL) and water (30 mL). The organic phase was washed with water (30 mL, 4 times) and dried over $MgSO_4$. After removal of the solvent, the resulting residue (98% crude yield) was purified by column chromatography over silica gel with *n*-hexane/EtOAc (4:1) to give (*S*)-**9** (2.43 g, 77%) as a yellow solid: $[\alpha]_D^{25}$=+4.45 (*c* 0.44, THF); ^{1}H NMR δ 0.80 (s, 9H), 5.50 (s, 1H), 7.16 (d, J=9.2 Hz, 1H), 7.23 (d, J=8.4 Hz, 1H), 7.39 (t, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.39 (d, J=8.8 Hz, 1H), 7.47 (d, J=8.8 Hz, 1H), 7.55 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 8.00–8.03 (m, 2H), 8.08 (d, J=9.2 Hz, 1H), 8.12 (d, J=8.8 Hz, 1H), 8.80 (d, J=2.4 Hz, 1H); ^{13}C NMR δ 26.55, 38.82, 114.90, 120.18, 120.47, 121.31, 121.81, 124.76, 125.97, 126.46, 127.22, 128.53, 131.46, 132.17, 132.31, 133.00, 136.63, 143.75, 148.35, 155.19, 177.55. Anal. calcd for $C_{25}H_{21}O_5N$: C, 72.28; H, 5.10; N, 3.37. Found: C, 72.46; H, 5.14; N, 3.40.

4.1.9. (*S*)-6-Nitro-2-methoxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-10). To a solution of (*S*)-**11** (2.075 g, 5.00 mmol) in acetone (40 mL) were added potassium carbonate (2.10 g, 15.0 mmol) and methyl iodide (1.45 g, 10.00 mmol), and the reaction mixture was refluxed for 18 h. After being cooled to ambient temperature, the reaction mixture was concentrated in vacuo. The residual oil was dissolved in ether and washed with water, 1N HCl, saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$ and concentrated in vacuo to give (*S*)-**12** (1.86 g, 87%) as an orange solid: $[\alpha]_D^{25}$=−6.5 (*c* 0.51, THF); ^{1}H NMR δ 0.75 (s, 9H), 3.83 (s, 3H), 7.17 (d, J=8.0 Hz, 1H), 7.23 (d, J=9.6 Hz, 1H), 7.31 (t, J=7.6 Hz, 1H), 7.39 (d, J=8.8 Hz, 1H), 7.48 (t, J=7.2 Hz, 1H), 7.55 (d, J=9.2 Hz, 1H), 7.95–7.99 (m, 2H), 8.17 (d, J=9.6 Hz, 1H), 8.82 (d, J=2.4 Hz, 1H); ^{13}C NMR δ 26.58, 38.66, 56.59, 114.99, 118.46, 119.88, 121.87, 123.69, 124.74, 125.35, 125.56, 126.70, 126.84, 126.88, 128.29, 129.57, 131.68, 132.21, 133.23, 136.56, 143.70, 146.99, 158.03, 176.07. Anal. calcd for $C_{26}H_{23}O_5N$: C, 72.71; H, 5.40; N, 3.26. Found: C, 72.66; H, 5.32; N, 3.41.

4.1.10. (*S*)-6-Nitro-2-methoxy-2′-hydroxy-1,1′-binaphthyl ((*S*)-11). A mixture of (*S*)-**10** (1.86 g, 4.33 mmol), potassium hydroxide (0.855 g, 15.0 mmol), THF (20 mL) and water (20 mL) was refluxed for 12 h. After being cooled to ambient temperature, the mixture was acidified with 1N HCl and extracted with EtOAc. The organic phase was washed with aqueous $NaHCO_3$ and brine, and dried over $MgSO_4$. The solvent was removed in vacuo to give (*S*)-**13** (1.35 g, 90%) as a reddish colored solid: $[\alpha]_D^{25}$=−2.97 (*c* 0.61, THF); ^{1}H NMR δ 3.87 (s, 3H), 4.81 (s, 1H), 6.93 (d, J=7.6 Hz, 1H), 7.21–7.36 (m, 4H), 7.63 (d, J=9.2 Hz, 1H), 7.88 (d, J=8.0 Hz, 1H), 7.93 (d, J=9.2 Hz, 1H), 8.00 (dd, J_1=9.6 Hz, J_2=2.4 Hz, 1H), 8.25 (d, J=9.2 Hz, 1H), 8.86 (d, J=2.4 Hz, 1H); ^{13}C NMR δ 56.67, 113.70, 115.28, 116.30, 117.56, 120.57, 123.49, 124.18, 125.08, 126.48, 126.74, 127.43, 128.27, 129.14, 130.35, 133.19, 133.36, 136.95, 144.04, 151.18, 158.82. Anal. calcd for $C_{21}H_{15}O_4N$: C, 73.04; H, 4.38; N, 4.06. Found: C, 72.99; H, 4.48; N, 4.01.

4.1.11. (*S*)-6-Nitro-6′-bromo-2-methoxy-2′-hydroxy-1,1′-binaphthyl ((*S*)-12). To a solution of (*S*)-**11** (1.35 g, 3.91 mmol) in a mixture of CH_2Cl_2/THF (20 mL/10 mL) was added bromine (0.40 mL, 7.82 mmol) at 0°C and the reaction was stirred for 1.5 h. After being quenched with aqueous Na_2SO_3, the reaction mixture was diluted with CH_2Cl_2 (200 mL). The organic phase was washed with saturated aqueous $NaHCO_3$, 1N HCl and brine, and dried over $MgSO_4$. After removal of the solvent, (*S*)-**12** (1.66 g, 100%) was obtained as an orange–brown solid: $[\alpha]_D^{25}$=+0.41 (*c* 0.53, THF); ^{1}H NMR δ 3.88 (s, 3H), 4.87 (s, 1H), 6.81 (d, J=9.2 Hz, 1H), 7.23 (d, J=9.2 Hz, 1H), 7.29 (dd, J_1=9.2 Hz, J_2=2.4 Hz, 1H), 7.36 (d, J=8.8 Hz, 1H), 7.63 (d, J=9.6 Hz, 1H), 7.84 (d, J=8.8 Hz, 1H), 8.00–8.04 (m, 2H), 8.26 (d, J=9.2 Hz, 1H), 8.86 (d, J=2.4 Hz, 1H); ^{13}C NMR δ 56.65, 114.01, 115.19, 115.58, 117.27, 118.75, 120.74, 125.13, 126.03, 126.18, 127.41, 129.38, 129.95, 130.18, 130.27, 131.92, 133.42, 136.74, 144.07, 151.51, 158.78. Anal. calcd for $C_{21}H_{14}O_4NBr$: C, 59.45; H, 3.33; N, 3.30. Found: C, 59.33; H, 3.40; N, 3.16.

4.1.12. (*S*)-6-((*E*)-1-(Hydroxycarbonyl)ethen-2-yl)-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-14). A mixture of (*S*)-**3** (3.60 g, 8.0 mmol), *n*-butyl acrylate (1.13 g, 8.8 mmol), tri-*n*-butylamine (7.40 g, 40.0 mmol), tri-*o*-tolylphosphine (122 mg, 0.40 mmol), palladium diacetate (44 mg, 0.20 mmol) and DMF (20 mL) was stirred at 130°C for 36 h under nitrogen. After being cooled to ambient temperature, ether (200 mL) was added and the mixture was extracted with 1N HCl (50 mL, 2 times), saturated aqueous $NaHCO_3$ (50 mL) and brine. The organic phase was dried over $MgSO_4$, concentrated in vacuo and the residue was purified by column chromatography over silica gel using *n*-hexane/EtOAc (5:1) to afford (*S*)-6-((*E*)-1-(*n*-butyloxycarbonyl)ethen-2-yl)-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-**13**) (3.26 g, 82%) as a pale yellow solid: $[\alpha]_D^{25}$=+49.42 (*c* 0.53, THF). Anal. calcd for $C_{32}H_{32}O_5$: C, 77.40; H, 6.50. Found: C, 77.15; H, 6.55. Though the product was analytically pure, ^{1}H NMR and ^{13}C NMR studies gave complicated spectra with overlapping signals. This material was taken on to the next hydrolysis without further spectroscopic studies. The enantiomeric purity of **13** was determined by HPLC analysis (see (*S*)-**20**). A mixture of (*S*)-**13** (400 mg, 0.806 mmol), potassium hydroxide (456 mg, 8.00 mmol), THF (15 mL) and water (10 mL) was stirred at 25°C for 16 h. The reaction mixture was acidified with 1N HCl (15 mL) and extracted with EtOAc (30 mL, 3 times). The combined organic phase was washed with brine, dried with $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography over silica gel using *n*-hexane/EtOAc (1:2) to give (*S*)-**14** (240 mg, 84%) as a yellow solid: $[\alpha]_D^{25}$=+94.6 (*c* 0.55, THF); ^{1}H NMR (DMSO-d_6) δ 6.47 (d, J=15.9 Hz, 1H), 6.93

(d, J=8.8 Hz, 1H), 6.94 (d, J=7.8 Hz, 1H), 7.18 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.25 (td, J_1=7.3 Hz, J_2=1.2 Hz, 1H), 7.32 (d, J=9.0 Hz, 1H), 7.36 (d, J=8.8 Hz, 1H), 7.54 (dd, J_1=9.0 Hz, J_2=1.7 Hz, 1H), 7.69 (d, J=15.9 Hz, 1H), 7.86 (m, 2H), 7.90 (d, J=8.8 Hz, 1H), 8.10 (d, J=1.7 Hz, 1H), 9.26 (s, 1H), 9.51 (s, 1H), 12.27 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 114.90, 115.92, 117.51, 118.49, 119.13, 122.29, 123.78, 124.21, 125.14, 125.93, 127.79, 127.87, 128.06, 128.36, 128.79, 129.55, 130.18, 133.97, 135.07, 144.31, 152.98, 154.48, 167.74. Anal. calcd for $C_{23}H_{16}O_4$: C, 77.52; H, 4.53. Found: C, 77.75; H, 4.49.

4.1.13. (*S*)-6-((*E*)-1-(*n*-Butyloxycarbonyl)ethen-2-yl)-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-15). A mixture of (*S*)-**3** (7.20 g, 19.73 mmol), *n*-butyl acrylate (2.82 g, 22.0 mmol), tri-*n*-butylamine (18.53 g, 100.0 mmol), tri-*o*-tolylphosphine (243 mg, 0.80 mmol), palladium diacetate (89.8 mg, 0.40 mmol) and DMF (100 mL) was stirred at 130°C for 36 h. After being cooled to ambient temperature, the reaction mixture was diluted with EtOAc (300 mL), and washed with 1N HCl (30 mL, 2 times), aqueous $NaHCO_3$ (5%, 30 mL, 2 times), water and brine. The organic phase was dried over $MgSO_4$ and concentrated in vacuo. The residue was purified by column chromatography over silica gel with *n*-hexane/EtOAc (2:1) to give (*S*)-**15** (7.72 g, 95%) as a yellow oil: $[\alpha]_D^{25}$=+5.38 (*c* 0.44, THF); ^{1}H NMR δ 0.88 (t, J=7.4 Hz, 3H), 1.32 (td, J_1=7.5 Hz, J_2=7.5 Hz, 2H), 1.56 (m, 2H), 2.67 (t, J=7.8 Hz, 2H), 3.06 (t, J=7.8 Hz, 2H), 4.06 (t, J=6.6 Hz, 2H), 5.04 (s, 1H), 5.08 (s, 1H), 7.07 (d, J=8.5 Hz, 1H), 7.14 (d, J=9.0 Hz, 1H), 7.16 (d, J=7.7 Hz, 1H), 7.29 (t, J=7.6 Hz, 1H), 7.34–7.39 (m, 3H), 7.69 (s, 1H), 7.88–7.90 (m, 2H), 7.96 (d, J=9.0 Hz, 1H); ^{13}C NMR δ 13.83, 19.28, 30.82, 64.50, 110.31, 111.63, 117.58, 117.87, 118.49, 123.95, 124.05, 124.96, 125.11, 125.15, 127.52, 128.39, 129.19, 129.38, 130.16, 131.55, 131.86, 133.26, 134.45, 144.21, 152.77, 153.80, 167.08. Anal. calcd for $C_{27}H_{24}O_4$: C, 78.62; H, 5.86. Found: C, 78.58; H, 5.66. The enantiomeric purity of **15** was determined by HPLC analysis with a chiral phase stationary column to be 22% (Daicel OD-H, *n*-hexane/isopropanol 9:1, flow 0.5 mL/min, (*S*)-**15** 44.9 min, (*R*)-**15** 61.8 min).

4.1.14. (*S*)-3,3′-Dimethyl-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-17). To a solution of (*S*)-3,3′-dimethyl-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-**16**) (4.082 g, 13.0 mmol) and triethylamine (5.42 mL, 39.0 mmol) in acetonitrile (40 mL) was added pivaloyl chloride (1.60 g, 13.26 mmol) dropwise over a period of 1 h at 0°C. The mixture was allowed to warm to 25°C and stirred for 4 h. The reaction mixture was diluted with ether and washed with aqueous 1N HCl (30 mL, 2 times), saturated aqueous $NaHCO_3$ (30 mL, 2 times) and brine (30 mL, 2 times). The organic phase was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (eluent: *n*-hexane/EtOAc=9/1) to give (*S*)-**17** (3.65 g, 70%) as a white solid: $[\alpha]_D^{25}$=−76.3 (*c* 0.55, THF); ^{1}H NMR δ 0.78 (s, 9H), 2.40 (s, 3H), 2.47 (s, 3H), 5.19 (s, 1H), 6.96 (d, J=8.4 Hz, 1H), 7.17 (t, J=7.4 Hz, 1H), 7.22–7.29 (m, 3H), 7.46 (t, J=7.2 Hz, 1H), 7.70 (s, 1H), 7.73 (d, J=8.4 Hz, 1H), 7.88 (d, J=8.4 Hz, 1H), 7.89 (s, 1H); ^{13}C NMR δ 17.08, 26.51, 38.85, 123.27, 125.40, 125.48, 126.07, 126.37, 126.94, 127.43, 128.90, 129.34, 130.38, 132.26, 147.96. Anal. calcd for $C_{27}H_{26}O_3$: C, 81.38; H, 6.38. Found: C, 81.27; H, 6.61.

4.1.15. (*S*)-6-Bromo-3,3′-dimethyl-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl ((*S*)-18). To a solution of pivalate (*S*)-**17** (1.99 g, 5.0 mmol) in acetonitrile (20 mL) was slowly added bromine (0.51 mL, 10.0 mmol) and the reaction mixture was stirred at 0°C for 1 h. The excess of bromine was quenched with aqueous Na_2SO_3. The colorless solution was diluted with ether (100 mL). The organic phase was washed with saturated aqueous $NaHCO_3$, aqueous 1N HCl, brine and then dried over $MgSO_4$. After removal of the solvent, (*S*)-**18** (2.36 g, 99%) was obtained as a light yellow solid: $[\alpha]_D^{25}$=−27.1 (*c* 0.60, THF); ^{1}H NMR δ 0.80 (s, 9H), 5.28 (s, 1H), 6.84 (d, J=8.8 Hz, 1H), 7.17 (d, J=8.8 Hz, 1H), 7.21–7.31 (m, 3H), 7.47 (td, J_1=7.4 Hz, J_2=1.2 Hz, 1H), 7.61 (s, 1H), 7.98 (m, 3H); ^{13}C NMR δ 17.03, 17.11, 26.54, 38.88, 117.03, 126.18, 126.52, 127.51, 128.38, 128.66, 128.91, 129.96, 130.65, 132.25, 147.94. Anal. calcd for $C_{27}H_{25}O_3Br$: C, 67.93; H, 5.28. Found: C, 67.75; H, 4.95.

4.1.16. (*S*)-6-Bromo-3,3′-dimethyl-2,2′-dihydroxy-1,1′-binaphthyl ((*S*)-19). To a solution of (*S*)-**18** (954 mg, 2.0 mmol) in ether (20 mL) was added DIBAL-H (1 M in toluene, 8.0 mL, 8.0 mmol) and the reaction mixture was stirred at 25°C overnight. The mixture was diluted with ether (100 mL), quenched with a small portion of water, and washed with aqueous 1N HCl (30 mL) and brine (30 mL, 2 times). The organic phase was dried over $MgSO_4$, and concentrated in vacuo. The residue was chromatographed on silica gel with *n*-hexane/EtOAc (6:1) to give (*S*)-**19** (733 mg, 93%) as a white solid: $[\alpha]_D^{25}$=−20.1 (*c* 0.55, THF); ^{1}H NMR δ 2.50 (s, 6H), 5.04 (s, 1H), 5.15 (s, 1H), 6.93 (d, J=9.2 Hz, 1H), 7.02 (d, J=8.4 Hz, 1H), 7.24 (td, J_1=7.2 Hz, J_2=1.2 Hz, 1H), 7.28 (dd, J_1=8.8 Hz, J_2=2.0 Hz, 1H), 7.34 (td, J_1=6.8 Hz, J_2=1.2 Hz, 1H), 7.70 (s, 1H), 7.80 (s, 1H), 7.82 (d, J=6.4 Hz, 1H), 7.96 (d, J=2.0 Hz, 1H); ^{13}C NMR δ 17.02, 17.11, 109.83, 110.78, 117.62, 123.77, 124.00, 125.90, 126.47, 126.97, 127.56, 129.38, 129.45, 129.52, 129.65, 130.49, 130.67, 130.92, 151.95, 152.24. Anal. calcd for $C_{22}H_{17}O_2Br$: C, 67.19; H, 4.36. Found: C, 66.97; H, 4.60.

4.1.17. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bishydroxy-1,1′-binaphthyl ((*S*)-20. A solution of (*S*)-**13** (see (*S*)-**14**) (2.48 g, 5.0 mmol), $Pd(OAc)_2$ (5 mg) in EtOAc (35 mL) was stirred at 60°C for 72 h under a hydrogen atmosphere. The catalyst was filtered off (Caution! Pyrophoric!), and the solvent was removed in vacuo. The residue was chromatographed on silica gel using *n*-hexane/EtOAc (5:1) giving 2.36 g (95%) of (*S*)-6-(2-*n*-butyloxycarbonyl)ethyl-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl as a white foam: $[\alpha]_D^{25}$=−20.71 (*c* 0.95, THF). Anal. calcd for $C_{32}H_{34}O_5$: C, 77.08; H, 6.87. Found: C, 76.97; H, 6.71. Though the product was analytically pure, ^{1}H NMR and ^{13}C NMR studies gave complicated spectra with overlapping signals. This material was taken on to the next hydrolysis without further spectroscopic studies. A mixture of (*S*)-6-(2-*n*-butyloxycarbonyl)ethyl-2-hydroxy-2′-pivaloyloxy-1,1′-binaphthyl (1.85 g, 3.71 mmol), potassium hydroxide (1.06 g, 18.60 mmol), THF (15 mL) and water (10 mL) were stirred at 25°C for 16 h. 1N HCl (50 mL) was added

and the mixture was extracted with EtOAc (40 mL, 3 times). The combined organic phases were extracted with brine and dried over $MgSO_4$. After removal of the solvent in vacuo the residue was chromatographed on silica gel using *n*-hexane/EtOAc (2:1) giving 1.26 g (95%) (*S*)-6-(2-hydroxycarbonyl)ethyl-2,2′-bishydroxy-1,1′-binaphthyl as a white glassy solid: $[\alpha]_D^{25}=+3.05$ (*c* 0.58, THF); ^{1}H NMR δ 2.72 (t, *J*=7.8 Hz, 2H), 3.06 (t, *J*=7.8 Hz, 2H), 5.05 (br s, 2H), 7.08 (d, *J*=8.8 Hz, 1H), 7.15 (m, 2H), 7.30 (td, J_1=6.8 Hz, J_2=1.6 Hz, 1H), 7.34–7.39 (m, 3H), 7.69 (d, *J*=1.2 Hz, 1H), 7.88 (d, *J*=7.6 Hz, 1H), 7.89 (d, *J*=8.8 Hz, 1H), 7.96 (d, *J*=8.8 Hz, 1H); ^{13}C NMR δ 30.41, 35.31, 110.78, 110.83, 117.69, 117.89, 123.96, 124.11, 124.51, 127.02, 127.40, 128.32, 128.36, 129.35, 129.48, 130.89, 131.31, 132.03, 133.30, 135.72, 152.33, 152.59, 177.80. Anal. calcd for $C_{23}H_{18}O_4$: C, 77.08; H, 5.06. Found: C, 77.13; H, 5.10. (*S*)-6-(2-Hydroxycarbonyl)ethyl-2,2′-bishydroxy-1,1′-binaphthyl (1.26 g, 3.52 mmol), trimethyl orthoformate (5 mL), THF (30 mL) and a mixture of MeOH (5 mL) and AcCl (0.3 mL) were stirred for 24 h at 25°C and then concentrated in vacuo. The residue was dissolved in EtOAc (100 mL) and washed with water, aqueous $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$. After removal of the solvent in vacuo the residue was chromatographed on silica gel with *n*-hexane/EtOAc (2:1) to give 1.30 g (99%) (*S*)-**20** as a white glassy foam: $[\alpha]_D^{25}=+3.67$ (*c* 0.52, THF); 98% ee (Daicel Chiracel OD-H, eluent: *n*-hexane/isopropanol 10:1, flow: 1 mL/min, *S*-enantiomer 27.4 min, *R*-enantiomer 33.9 min); ^{1}H NMR δ 2.68 (t, *J*=8.0 Hz, 2H), 3.06 (t, *J*=8.0 Hz, 2H), 3.66 (s, 3H), 5.04 (s, 1H), 5.08 (s, 1H), 7.08 (d, *J*=8.4 Hz, 1H), 7.15 (m, 2H), 7.30 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.34–7.39 (m, 3H), 7.69 (s, 1H), 7.88 (m, 2H), 7.96 (d, *J*=9.2 Hz, 1H); ^{13}C NMR δ 30.68, 35.50, 51.62, 110.66, 110.77, 117.60, 117.77, 123.86, 124.04, 124.35, 126.93, 127.30, 128.24, 128.33, 129.26, 129.42, 130.80, 131.21, 131.90, 133.22, 136.00, 152.23, 152.52, 173.09. Anal. calcd for $C_{24}H_{20}O_4$: C, 77.40; H, 5.41. Found: C, 77.61; H, 5.51.

4.1.18. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bis-(trifluoromethanesulfonyl)-1,1′-binaphthyl ((*S*)-21). To a solution of (*S*)-**20** (2.20 g, 5.91 mmol) pyridine (1.44 mL, 17.73 mmol) in CH_2Cl_2 was added triflic anhydride (2.17 mL, 13.01 mmol) at 0°C. The reaction mixture was stirred overnight. To the reaction mixture was added water (50 mL), and the organic phase was washed with aqueous 1N HCl. The organic phase was dried over Na_2SO_4 and concentrated in vacuo. The residue was chromatographed on silica gel with *n*-hexane/EtOAc (5:1) to give 3.37 g of (*S*)-**21** (90%) as yellow oil; $[\alpha]_D^{25}=+114.51$ (*c* 0.725, THF); ^{1}H NMR δ 2.73 (t, *J*=7.8 Hz, 2H), 3.12 (t, *J*=7.8 Hz, 2H), 3.67 (s, 3H), 7.17 (d, *J*=8.8 Hz, 1H), 7.25–7.27 (m, 2H), 7.40 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.56–7.62 (m, 3H), 7.80 (s, 1H), 8.00 (d, *J*=8.0 Hz, 1H), 8.06 (d, *J*=8.8 Hz, 1H), 8.13 (d, *J*=9.2 Hz, 1H); ^{13}C NMR δ 30.84, 35.16, 51.74, 116.46, 119.21, 119.42, 119.65, 123.20, 123.39, 126.68, 126.80, 126.88, 127.22, 127.87, 128.24, 129.05, 131.42, 131.73, 131.87, 132.24, 132.46, 133.04, 139.65, 144.95, 145.25, 172.91. Anal. calcd for $C_{26}H_{22}O_8S_2F_6$: C, 48.75; H, 3.46. Found: C, 48.49; H, 3.39.

4.1.19. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bis-(methoxycarbonyl)-1,1′-binaphthyl ((*S*)-22. A pressure bottle was charged with (*S*)-**21** (3.32 g, 5.22 mmol), palladium(II) acetate (116 mg, 0.52 mmol), dppp (214 mg, 0.52 mmol), diisopropylethylamine (4.5 mL), MeOH (10 mL) and DMSO (30 mL). The mixture was stirred at 120°C for 72 h under carbon monoxide (5 atm). After being cooled, the reaction mixture was diluted with EtOAc (150 mL). The mixture was washed with aqueous 1N HCl (50 mL, 2 times), saturated aqueous $NaHCO_3$ (30 mL), brine, and dried with $MgSO_4$. The solvent was removed in vacuo and the residue was chromatographed on silica gel (eluent: *n*-hexane/EtOAc (2:1)) to give 1.75 g of (*S*)-**22** (73%) as light yellow foam; $[\alpha]_D^{25}=+0.44$ (*c* 0.70, THF); >98% ee (HPLC, Daicel Chiracel OD-H, eluent: *n*-hexane/isopropanol=10/1, flow: 0.5 mL/min, *S*-enantiomer 32.6 min, *R*-enantiomer 28.5 min), ^{1}H NMR δ 2.69 (t, *J*=7.8 Hz, 2H), 3.07 (t, *J*=7.8 Hz, 2H), 3.48 (s, 3H), 3.50 (s, 3H), 3.67 (s, 3H), 6.98 (d, *J*=8.8 Hz, 1H), 7.06 (d, *J*=9.5 Hz, 1H), 7.08 (d, *J*=7.1 Hz, 1H), 7.23 (td, J_1=7.7 Hz, J_2=1.2 Hz, 1H), 7.51 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.73 (s, 1H), 7.93 (d, *J*=8.8 Hz, 2H), 8.00 (d, *J*=8.8 Hz,1H), 8.17 (m, 2H); ^{13}C NMR δ 30.84, 35.07, 51.67, 51.80, 51.85, 125.87, 126.17, 126.53, 126.68, 127.07, 127.26, 127.45, 127.51, 127.65, 127.82, 127.93, 131.63, 132.88, 134.82, 135.06, 140.07, 140.18, 140.38, 167.09, 167.10, 173.16. Anal. calcd for $C_{28}H_{24}O_6$: C, 73.67; H, 5.30. Found: C, 73.60; H, 5.26.

4.1.20. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bis-(hydroxycarbonyl)-1,1′-binaphthyl ((*S*)-23). A mixture of (*S*)-**22** (990 mg, 2.17 mmol) and potassium hydroxide (618 mg, 10.85 mmol) were refluxed in a mixture of THF (20 mL) and water (10 mL) for 20 h. After being cooled, the mixture was concentrated in vacuo to remove THF. The aqueous residue was diluted with aqueous 1N HCl (30 mL) and the mixture was extracted with EtOAc (50 mL, 2 times). The combined organic phase was washed with brine, dried over $MgSO_4$, and concentrated to give 890 mg of (*S*)-6-(2-hydroxycarbonyl)ethyl-2,2′-bis(hydroxycarbonyl)-1,1′-binaphthyl (99%) as a white solid; $[\alpha]_D^{25}=-1.09$ (*c* 0.52, THF); ^{1}H NMR (DMSO) δ 2.61 (t, *J*=7.7 Hz, 2H), 2.95 (t, *J*=7.7 Hz, 2H), 6.79 (d, *J*=8.8 Hz, 1H), 6.88 (d, *J*=8.5 Hz, 1H), 7.19 (dd, J_1=8.8 Hz, J_2=1.7 Hz, 1H), 7.28 (td, J_1=7.7 Hz, J_2=1.5 Hz, 1H), 7.55 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.85 (d, *J*=1.0 Hz,1H), 7.98–8.12 (m, 5H), 12.25 (br, 3H); ^{13}C NMR δ 30.25, 34.57, 126.00, 126.20, 126.25, 126.62, 126.67, 127.03, 127.36, 127.42, 127.90, 127.91, 128.02, 131.10, 132.47, 134.25, 134.47, 139.33, 139.52, 140.26, 167.59, 167.64, 173.64. Anal. calcd for $C_{25}H_{18}O_6$: C, 72.46; H, 4.38. Found: C, 72.21; H, 4.18. To a solution of the triacid (890 mg, 2.15 mmol), trimethyl orthoformate (3 mL) in THF (30 mL) was added MeOH (5 mL) and AcCl (0.3 mL). The mixture was stirred for 24 h at 25°C. The solvent was removed in vacuo, the residue was dissolved in EtOAc (20 mL). The solution was extracted with aqueous $NaHCO_3$. The aqueous phase was acidified with 1N HCl and extracted with EtOAc (50 mL, 2 times). The combined organic phase was extracted with brine and dried over $MgSO_4$. After removal of the solvent, 870 mg of (*S*)-**23** was obtained as white solid (94%); $[\alpha]_D^{25}=+0.75$ (*c* 0.59, THF); ^{1}H NMR δ 2.65 (t, *J*=7.8 Hz, 2H), 3.03 (t, *J*=7.8 Hz, 2H), 3.64 (s, 3H), 6.80 (d, *J*=8.8 Hz, 1H), 6.87 (d, *J*=8.4 Hz,1H), 6.98 (td, J_1=8.8 Hz, J_2=1.6 Hz, 1H), 7.47 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.68 (s, 1H),

7.85–7.94 (m, 3H), 8.07 (d, J=8.4 Hz, 1H), 8.09 (d, J=8.4 Hz, 1H), 12.34 (br, 2H); ^{13}C NMR δ 30.90, 35.08, 51.72, 125.08, 125.48, 126.36, 126.50, 126.64, 127.29, 127.35, 127.54, 127.64, 127.73, 127.77, 127.87, 131.46, 132.70, 135.22, 135.46, 140.31, 141.40, 141.57, 171.82, 173.06. Anal. calcd for $C_{26}H_{20}O_6$: C, 72.89; H, 4.71. Found: C, 73.00; H, 4.75.

4.2. General procedure for the preparation of amides 25a–d

To a solution of (*S*)-**23** (1 equiv.) and oxalyl chloride (5 equiv.) in CH_2Cl_2 was added a catalytic amount (trace) of DMF at 0°C and stirred 5 h. The mixture was concentrated in vacuo to remove the solvent and the excess of oxalyl chloride. The resulting crude acid chloride was dissolved in CH_2Cl_2. The solution was added to a mixture of amino alcohol (2 equiv.) and triethylamine (3 equiv.) in CH_2Cl_2 at 0°C. The reaction mixture was stirred overnight at 25°C. The mixture was diluted with chloroform and was washed with aqueous 1N HCl, saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$ and concentrated in vacuo. The residue was chromatographed on silica gel (eluent: $CHCl_3$/MeOH or *n*-hexane/EtOAc).

4.2.1. (*S*)-6-(2-Methoxycarbonylethyl)-2,2′-bis[((*S*)-1-isopropyl-2-hydroxyethylamino)carbonyl]-1,1′-binaphthyl ((*S*,*S*)-25a). Yield: 61% white solid; $[\alpha]_D^{25}=-151.34$ (*c* 0.54, THF); ^{1}H NMR δ 0.50 (d, J=6.4 Hz, 6H), 0.62 (m, 6H), 1.53 (oct, J=6.8 Hz, 2H), 1.84 (s, br, 2H), 2.68 (t, J=7.9 Hz, 2H), 3.07 (t, J=7.9 Hz, 2H), 3.22 (m, 4H), 3.52 (m, 2H), 3.67 (s, 3H), 6.98 (s, br, 1H), 7.08 (s, br, 1H), 7.15–7.21 (m, 3H), 7.32 (td, J_1=7.7 Hz, J_2=1.2 Hz, 1H), 7.49 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.67 (m, 3H), 7.93 (d, J=8.3 Hz, 1H), 7.95 (d, J=8.3 Hz, 1H), 8.01 (d, J=8.3 Hz, 1H); ^{13}C NMR δ 18.24, 18.30, 19.07, 19.12, 28.72, 30.85, 35.25, 51.70, 57.14, 57.21, 63.32, 63.46, 123.80, 124.02, 126.57, 126.80, 126.90, 127.17, 127.48, 128.23, 128.62, 128.68, 129.07, 131.32, 132.50, 132.67, 133.81, 134.05, 139.56, 170.87, 170.95, 173.17. Anal. calcd for $C_{36}H_{42}O_6N_2$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.28; H, 7.01; N, 4.59.

4.2.2. (*S*)-6-(2-Methoxycarbonylethyl)-2,2′-bis[((*S*)-1-phenyl-2-hydroxyethylamino)carbonyl]-1,1′-binaphthyl ((*S*,*S*)-25b). Yield: 95%, white solid; $[\alpha]_D^{25}=-133.61$ (*c* 0.51, THF); ^{1}H NMR δ 2.18 (s, br, 2H), 2.71 (t, J=7.6 Hz, 2H), 3.10 (t, J=7.4 Hz, 2H), 3.41 (m, 4H), 3.63 (s, 3H), 4.81 (m, 2H), 6.72 (m, 4H), 7.08–7.40 (m, 12H), 7.54 (td, J_1=7.0 Hz, J_2=1.2 Hz, 1H), 7.69 (d, J=8.4 Hz, 1H), 7.71 (d, J=8.8 Hz, 1H), 7.76 (s, 1H), 7.95 (d, J=8.4 Hz, 1H), 7.98 (d, J=8.4 Hz, 1H), 8.02 (d, J=8.4 Hz, 1H); ^{13}C NMR δ 30.93, 35.25, 51.76, 55.67, 55.71, 65.72, 65.80, 124.06, 124.19, 126.36, 126.45, 126.52, 126.68, 126.76, 126.83, 127.21, 127.27, 127.30, 127.53, 128.27, 128.36, 128.41, 128.66, 128.81, 128.87, 129.09, 131.33, 132.44, 132.57, 132.74, 133.81, 134.03, 134.42, 134.84, 138.20, 138.41, 139.60, 169.99, 170.05, 173.13. Anal. calcd for $C_{42}H_{38}O_6N_2$: C, 75.66; H, 5.74; N, 4.20. Found: C, 75.71; H, 5.85; N, 4.18.

4.2.3. (*S*)-6-(2-Methoxycarbonylethyl)-2,2′-bis[((*S*)-1-*tert*-buthyl-2-hydroxyethylamino)carbonyl]-1,1′-binaphthyl ((*S*,*S*)-25c). Yield: 70% white solid; $[\alpha]_D^{25}=-99.60$ (*c* 0.55, THF); ^{1}H NMR δ 0.65 (s, 9H), 0.67 (s, 9H), 1.67 (s, br, 2H), 2.68 (t, J=7.9 Hz, 2H), 3.07 (t, J=7.9 Hz, 2H), 3.15 (m, 2H), 3.53 (m, 2H), 3.66 (s, 3H), 3.67 (m, 2H), 7.02 (d, J=9.8 Hz, 1H), 7.10 (d, J=9.8 Hz, 1H), 7.19 (s, 2H), 7.25 (d, J=8.2 Hz, 1H), 7.33 (td, J_1=7.7 Hz, J_2=1.2 Hz, 1H), 7.49 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.67 (m, 2H), 7.72 (s, 1H), 7.92 (d, J=8.3 Hz, 1H), 7.94 (d, J=8.6 Hz, 1H), 8.01 (d, J=8.3 Hz, 1H); ^{13}C NMR δ 26.46, 26.49, 30.80, 33.31, 33.38, 35.20, 51.66, 59.38, 59.48, 62.30, 62.38, 123.75, 123.98, 126.72, 126.80, 127.07, 127.14, 127.41, 128.15, 128.48, 128.54, 128.92, 131.48, 132.70, 132.83, 132.92, 133.69, 133.92, 135.00, 135.48, 139.46, 171.26, 171.36, 173.13. Anal. calcd for $C_{38}H_{46}O_6N_2$: C, 72.82; H, 7.40; N, 4.47. Found: C, 73.03; H, 7.31; N, 4.31.

4.2.4. (*S*)-6-(2-Methoxycarbonylethyl)-2,2′-bis[(1,1-dimethyl-2-hydroxyethylamino)carbonyl]-1,1′-binaphthyl ((*S*)-25d). Yield: 89% white solid; $[\alpha]_D^{25}=-168.80$ (*c* 0.56, THF); ^{1}H NMR δ 0.57 (s, 3H), 0.64 (s, 3H), 0.74 (s, 3H), 0.81 (s, 3H), 2.69 (t, J=8.8 Hz, 2H), 3.08–3.19 (m, 6H), 3.65 (s, 3H), 3.98 (s, br, 2H), 6.71 (s, 1H), 6.83 (s, 1H), 7.15–7.27 (m, 4H), 7.35 (t, J=7.6 Hz, 1H), 7.53 (t, J=7.5 Hz, 1H), 7.70 (m, 2H), 7.74 (s, 1H), 7.95 (d, J=8.5 Hz, 1H), 7.97 (d, J=8.6 Hz, 1H), 8.01 (d, J=8.6 Hz, 1H); ^{13}C NMR δ 22.66, 23.10, 23.60, 23.71, 30.85, 35.27, 51.73, 56.11, 56.31, 69.90, 69.93, 123.79, 124.26, 126.34, 126.69, 126.85, 127.25, 127.47, 128.29, 128.57, 128.63, 129.03, 131.00, 132.16, 132.23, 132.53, 133.90, 134.19, 134.79, 135.28, 139.59, 170.51, 170.66, 173.26. Anal. calcd for $C_{34}H_{40}O_6N_2$: C, 71.31; H, 7.04; N, 4.89. Found: C, 71.10; H, 7.03; N, 4.85.

4.3. General procedure for the preparation of oxazolines 26a–d

To a mixture of the amide (1.0 equiv.) and diisopropylethylamine (1.5 equiv.) in CH_2Cl_2, was added methanesulfonic chloride (1.1 equiv.) at 0°C. The mixture was stirred overnight at 25°C. The mixture was diluted with $CHCl_3$, and washed with aqueous 1N HCl, saturated aqueous $NaHCO_3$ and brine. The organic phase was dried over $MgSO_4$. After removal of the solvent in vacuo the residue was chromatographed on silica gel to give **26**.

4.3.1. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bis((*S*)-4-isopropyloxazol-2-yl)-1,1′-binaphthyl ((*S*,*S*)-26a). Yield: 82% white solid; $[\alpha]_D^{25}=-97.75$ (*c* 0.75, THF); ^{1}H NMR δ 0.58 (m, 12H), 1.30 (m, 2H), 2.68 (t, J=7.8 Hz, 2H), 3.07 (t, J=7.8 Hz, 2H), 3.56–3.75 (m, 6H), 3.67 (s, 3H), 7.05 (dd, J_1=8.6 Hz, J_2=1.5 Hz, 1H), 7.11 (d, J=8.8 Hz, 1H), 7.17–7.23 (m, 2H), 7.45 (td, J_1=7.3 Hz, J_2=1.5 Hz, 1H), 7.68 (s, 1H), 7.86 (d, J=8.8 Hz, 1H), 7.88 (d, J=8.3 Hz, 1H), 7.93 (d, J=8.6 Hz, 1H), 8.08 (d, J=8.6 Hz, 1H), 8.09 (d, J=8.6 Hz, 1H); ^{13}C NMR δ 18.09, 18.11, 18.47, 18.50, 30.87, 32.62, 32.66, 35.32, 51.64, 69.97, 72.39, 125.39, 125.75, 126.13, 126.24, 126.30, 126.39, 126.69, 127.09, 127.12, 127.28, 127.41, 127.46, 127.69, 131.75, 132.97, 134.20, 134.42, 137.76, 137.97, 138.99, 163.75, 173.22. Anal. calcd for $C_{36}H_{38}O_4N_2$: C, 76.84; H, 6.81; N, 4.98. Found: C, 76.65; H, 6.78; N, 4.88.

4.3.2. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bis((*S*)-4-phenyloxazol-2-yl)-1,1′-binaphthyl ((*S*,*S*)-26b). Yield:

95% white solid; $[\alpha]_D^{25}=-16.93$ (*c* 0.48, THF); ^{1}H NMR δ 2.71 (t, *J*=7.8 Hz, 2H), 3.11 (t, *J*=7.8 Hz, 2H), 3.67 (s, 3H), 3.73 (m, 2H), 4.20 (m, 2H), 5.05 (m, 2H), 6.68–6.73 (m, 4H), 7.05–7.30 (m, 10H), 7.52 (td, J_1=7.4 Hz, J_2=1.2 Hz, 1H), 7.74 (s, 1H), 7.90 (d, *J*=8.8 Hz, 1H), 7.94 (d, *J*=8.0 Hz, 1H), 7.96 (d, *J*=8.8 Hz, 1H), 8.16 (d, *J*=8.8 Hz, 1H), 8.18 (d, *J*=8.8 Hz, 1H); ^{13}C NMR δ 30.94, 35.27, 51.71, 69.77, 74.43, 74.47, 125.15, 125.54, 126.16, 126.29, 126.32, 126.37, 126.41, 126.50, 126.88, 126.93, 127.06, 127.25, 127.35, 127.55, 127.62, 127.82, 128.19, 128.20, 131.68, 132.92, 134.35, 134.56, 137.83, 138.03, 139.23, 142.37, 142.39, 165.05, 165.10, 173.09. Anal. calcd for $C_{42}H_{34}O_4N_2$: C, 79.98; H, 5.43; N, 4.44. Found: C, 80.05; H, 5.38; N, 4.41.

4.3.3. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bis((*S*)-4-*tert*-butyloxazol-2-yl)-1,1′-binaphthyl ((*S*,*S*)-26c). Yield: 79% white solid; $[\alpha]_D^{25}=-54.95$ (*c* 0.58, THF); ^{1}H NMR δ 2.66 (t, *J*=8.0 Hz, 2H), 3.0 (t, *J*=8.0 Hz, 2H), 3.66 (s, 3H), 3.67 (m, 6H), 7.03 (dd, J_1=8.8 Hz, J_2=1.7 Hz, 1H), 7.07 (d, *J*=8.8 Hz,1H), 7.14 (d, *J*=8.6 Hz, 1H), 7.18 (td, J_1=7.6 Hz, J_2=1.2 Hz, 1H), 7.43 (td, J_1=7.4 Hz, J_2=1.4 Hz, 1H), 7.67 (d, *J*=1.2 Hz, 1H), 7.85 (d, *J*=8.8 Hz, 1H), 7.88 (d, *J*=8.3 Hz, 1H), 7.92 (d, *J*=8.8 Hz, 1H), 8.10 (d, *J*=8.6 Hz, 1H), 8.11 (d, *J*=8.6 Hz, 1H); ^{13}C NMR δ 25.47, 30.95, 33.56, 35.44, 51.67, 68.06, 76.01, 76.04, 125.08, 125.42, 125.98, 126.11, 126.19, 126.25, 126.58, 126.88, 127.10, 127.15, 127.25, 127.39, 127.56, 131.75, 132.97, 134.17, 134.40, 138.06, 138.28, 138.87, 163.01, 163.06, 173.10. Anal. calcd for $C_{38}H_{42}O_4N_2$: C, 77.26; H, 7.17; N, 4.74. Found: C, 77.09; H, 7.25; N, 4.67.

4.3.4. (*S*)-6-(2-Methoxycarbonyl)ethyl-2,2′-bis(4,4-dimethyloxazol-2-yl)-1,1′-binaphthyl ((*S*)-26d). Yield: 82% white solid; $[\alpha]_D^{25}=-7.28$ (*c* 0.49, THF); ^{1}H NMR δ 0.94 (s, 3H), 0.96 (s, 3H), 1.11 (s, 3H), 1.12 (s, 3H), 2.69 (t, *J*=7.8 Hz, 2H), 3.08 (t, *J*=7.8 Hz, 2H), 3.24 (m, 2H), 3.50 (m, 2H), 3.66 (s, 3H), 7.12 (dd, J_1=8.8 Hz, J_2=1.5 Hz, 1H), 7.20 (d, *J*=8.8 Hz,1H), 7.27 (m, 2H), 7.48 (m, 1H), 7.70 (m, 1H), 7.87 (d, *J*=8.6 Hz, 1H), 7.91 (d, *J*=7.8 Hz, 1H), 7.94 (d, *J*=8.6 Hz, 1H), 7.98 (m, 2H); ^{13}C NMR δ 27.97, 28.00, 30.99, 35.38, 51.76, 66.92, 79.38, 79.41, 126.00, 126.34, 126.41, 126.54, 126.62, 126.85, 127.46, 127.58, 127.76, 127.84, 127.94, 131.71, 132.95, 134.14, 134.36, 137.01, 137.24, 139.17, 163.70, 173.33. Anal. calcd for $C_{34}H_{36}O_4N_2$: C, 76.09; H, 6.76; N, 5.22. Found: C, 76.15; H, 6.82; N, 5.05.

4.4. Typical procedure for the immobilization of the boxax ligands

A mixture of boxax methyl ester **26** (1.00 equiv.) and $LiOH{\cdot}H_2O$ (1.05 equiv.) in THF/H_2O for 24 h at 25°C. The mixture was concentrated in vacuo to give the corresponding lithium carboxylate as white precipitates. Argo gel NH_2 (0.37 mmol/g, 1 equiv.) was washed with CH_2Cl_2, MeOH, MeCN and again CH_2Cl_2. After being dried in vacuo, the gel beads were swollen in DMF. A DMF solution of lithium carboxylate thus prepared (1.1 equiv.), HOBt (1.0 equiv.) and EDCI (2.5 equiv.) was added to the gel beads. The mixture was shaken for 12 h at 25°C, again EDCI (5 equiv.) was added and shaken for additional 24 h. The reaction mixture was filtered and the collected beads were washed with DMF, MeOH and CH_2Cl_2. The quantity of the coupling reaction was proved by the Kaiser test.[20] A negative Kaiser test and ^{13}C MASNMR studies indicated the complete consumption of the terminal amino residue of the starting resin and the exclusive formation of the desired PS–PEG supported boxax ligands. The loading value of the polymer-supported boxax ligands were estimated to be 0.30 mmol/g based on the initial loading value of the amino residue.

4.4.1. PS–PEG-(*S*,*S*)-ip-boxax (27a). ^{13}C-SR-MAS δ 17.92, 18.25, 31.35, 32.36, 37.33, 39.01, 69.64, 72.08, 124.86, 125.39, 131.29, 132.62, 133.79, 134.04, 134.12, 137.33, 137.63, 139.31, 163.31, 171.63.

4.4.2. PS–PEG-(*S*,*S*)-ph-Boxax (27b). ^{13}C-SR-MAS δ 31.26, 37.12, 38.94, 74.10, 131.23, 132.58, 133.97, 134.27, 137.46, 137.81, 139.70, 142.05, 164.68, 171.68.

4.4.3. PS–PEG-(*S*,*S*)-tb-Boxax (27c). ^{13}C-SR-MAS δ 25.21, 31.34, 33.27, 37.43, 39.00, 67.74, 75.75, 124.66, 125.18, 131.39, 132.69, 133.95, 134.18, 137.74, 137.81, 138.02, 139.28, 162.75, 171.68.

4.4.4. PS–PEG-(*S*)-dm-Boxax (27d). ^{13}C-SR-MAS δ 27.67, 31.30, 37.29, 39.00, 66.53, 78.96, 125.40, 131.17, 132.50, 133.60, 133.88, 136.54, 136.82, 139.35, 163.06, 171.59.

4.4.5. PS-(*S*,*S*)-ph-Boxax (28). ^{13}C-SR-MAS δ 31.52, 37.56, 74.23, 131.55, 132.82, 134.24, 134.45, 137.80, 137.99, 139.75, 142.24, 164.85, 171.37.

4.4.6. PEGA-(*S*,*S*)-ph-Boxax (29). ^{13}C-SR-MAS δ 31.77, 131.69, 133.03, 134.41, 134.62, 137.91, 138.16, 139.98, 142.48, 165.10, 171.23.

4.4.7. MeO–PEG-(*S*,*S*)-ph-Boxax (30). A solution of (*S*,*S*)-**26b** (1.1 equiv.) and $LiOH{\cdot}H_2O$ (1.15 equiv.) in a mixture of THF/H_2O was stirred for 24 h at 25°C. The mixture was concentrated in vacuo to give crude lithium carboxylate as white precipitates. $MeO-PEG_{5000}-NH_2$ (Fluka, 0.17 mmol/g, 1.00 equiv.), HOBt (2.5 equiv.) and EDCI (2.5 equiv.) were added to a acetonitrile solution (20 mL) of the lithium carboxylate thus prepared. The solution was stirred at ambient temperature for 18 h. EDCI (5 equiv.) was added to the reaction mixture and the reaction mixture was stirred for additional 24 h. To the mixture was added an excess amount of AcCl/Et_3N. After removal of the solvent, the crude solid was purified by recrystallization from MeOH. Yield: 85%, light yellow solid (loading 0.15 mmol/g). ^{1}H NMR δ 2.56 (t, *J*=7.8 Hz, 2H), 3.13 (t, *J*=7.8 Hz, 2H), 4.21 (m, 2H), 5.05 (m, 2H), 6.01 (t, *J*=7.0 Hz, 1H), 6.68–6.73 (m, 4H), 7.07–7.30 (m, 10H), 7.52 (td, J_1=7.4 Hz, J_2=1.2 Hz, 1H), 7.76 (s, 1H), 7.90 (d, *J*=8.8 Hz, 1H), 7.94 (d, *J*=8.0 Hz, 1H), 7.96 (d, *J*=8.8 Hz, 1H), 8.16 (d, *J*=8.8 Hz, 1H), 8.18 (d, *J*=8.8 Hz, 1H); ^{13}C NMR δ 31.61, 37.72, 39.29, 59.03, 125.53, 126.27, 126.31, 126.44, 126.91, 127.22, 127.68, 127.82, 128.19, 131.61, 134.33, 134.57, 137.81, 138.07, 139.84, 142.38, 165.05.

4.5. General procedure for the asymmetric Wacker-type cyclization of 31

A mixture of immobilized catalyst (0.02 mmol Pd), 2-(2,3-dimethyl-2-butenyl)-phenol (**31**) (0.2 mmol, 35.2 mg),

benzoquinone (0.8 mmol, 86.4 mg) and MeOH (1 mL) was agitated at 60°C with shaking for 20 h. After being cooled to room temperature, the resin was filtered off and washed twice with MeOH (1 mL). The solvent was removed in vacuo and the residue was purified by column chromatography using silica gel and *n*-hexane/EtOAc (95:5) giving (*S*)-2-isopropenyl-2-methyl-2,3-dihydrobenzofuran (**32**) as colorless oil. The enantiomeric excess was determined by GC (chiral stationary phase capillary column Cyclodex CB).[11]

Acknowledgements

This work was partially supported by a Grant-in-Aid for Creative Scientific Research (No. 13GS0024), Japan Society for the Promotion of Science, Grant-in-Aid for Scientific Research, the Ministry of Education and Science, Japan, the Asahi Glass Science Foundation, the Toray Foundation and the Sumitomo Foundation.

References

1. For reviews, see: (a) Rosini, C.; Franzini, L.; Raffaelli, A.; Salvadori, P. *Synthesis* **1992**, 503. (b) In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; Wiley-VCH: Weinheim, 2000; and references therein.
2. For reviews, see: (a) In *Chiral Catalyst Immobilization and Recycling*. De Vos, D. E., Vankelecom, I. F. J., Jacobs, P. A., Eds.; Wiley-VCH: Weinheim, 2000; and references cited therein. (b) Doerwald, F. Z. *Organic Synthesis on Solid Phase*; Wiley-VCH: Weinheim, 2000.
3. For recent examples of the immobilization of binaphthyl-based chiral catalysts, see: (a) Nozaki, K.; Itoi, Y.; Shibahara, F.; Shirakawa, E.; Ohta, T.; Takaya, H.; Hiyama, T. *J. Am. Chem. Soc.* **1998**, *120*, 4051. (b) Nozaki, K.; Itoi, Y.; Shibahara, F.; Shirakawa, E.; Ohta, T.; Takaya, H.; Hiyama, T. *Bull. Chem. Soc. Jpn* **1999**, *72*, 1911. (c) Bayston, D. J.; Fraser, J. L.; Ashton, M. R.; Baxter, A. D.; Polywka, M. E. C.; Moses, E. *J. Org. Chem.* **1998**, *63*, 3137. (d) Kobayashi, S.; Kusakabe, K.; Ishitani, H. *Org. Lett.* **2000**, *2*, 1225. (e) Fujii, A.; Sodeoka, M. *Tetrahedron Lett.* **1999**, *40*, 8011. (f) Matsunaga, S.; Ohshima, T.; Shibasaki, M. *Tetrahedron Lett.* **2000**, *41*, 8473. (g) Nogami, H.; Matsunaga, S.; Kanai, M.; Shibasaki, M. *Tetrahedron Lett.* **2001**, *42*, 279. (h) Takamura, M.; Funabashi, K.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2001**, *123*, 6801.
4. (a) Kawashima, M.; Kakayama, M. Japan Patent J P 200044504 assigned to Kankyo Kagaku Center K.K., Japan, 2000. (b) De Vanis, J.-B. R. *Tetrahedron Lett.* **2001**, *42*, 6507.
5. Asymmetric Wacker-type cyclization with the various immobilized boxax ligands has been reported, see: Hocke, H.; Uozumi, Y. *Synlett* **2002**, 2049.
6. During preparation of this manuscript, controlled monobromination of 1,1′-bi-2-naphthol via the monopivalate **2** was reported, see: Cai, D.; Larsen, R. D.; Reider, P. J. *Tetrahedron Lett.* **2002**, *43*, 4055.
7. Glaser, R.; Twaik, M. *Tetrahedron Lett.* **1976**, *15*, 1219.
8. Arnold, L. A.; Imbos, R.; Mandoli, A.; de Vries, A. H. M.; Naasz, R.; Feringa, B. L. *Tetrahedron* **2000**, *56*, 2865.
9. Brisdon, J. B.; England, R.; Reza, K.; Sainsbury, M. *Tetrahedron* **1993**, *49*, 1103.
10. Uozumi, Y.; Kyota, H.; Kishi, E.; Kitayama, K.; Hayashi, T. *Tetrahedron: Asymmetry* **1996**, *7*, 1603.
11. (a) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Am. Chem. Soc.* **1997**, *119*, 5063. (b) Uozumi, Y.; Kato, K.; Hayashi, T. *J. Org. Chem.* **1998**, *63*, 5071. (c) Uozumi, Y.; Kyota, H.; Hayashi, T. *J. Org. Chem.* **1999**, *64*, 1621.
12. (a) Hotta, H.; Suzuki, T.; Miyano, S.; Inoue, Y. *J. Mol. Cat.* **1989**, *54*, L5. (b) Ohta, T.; Ito, M.; Inagaki, K.; Takaya, H. *Tetrahedron Lett.* **1993**, *34*, 1615.
13. ArgoGel amino resin (1% DVB cross-linked) purchased from Argonaut Technologies Inc. was used.
14. Aminomethylated polystyrene (1% DVB cross-linked) was purchased from Novabiochem.
15. For a copolymerisate of acrylamidopropyl[2-aminopropyl]-polyethylene glycol and *N*,*N*-dimethylacrylamide crosslinked with bis(2-acrylamidopropyl)poly(ethylene glycol) (PEGA), see: Meldal, M. *Tetrahedron Lett.* **1992**, *33*, 3077.
16. MeO–PEG5000 amino resin was purchased from Fluka.
17. For reviews of PEG-supported reagents, see: (a) Sieber, F.; Wentworth, P.; Janda, K. D. *J. Comb. Chem.* **1999**, *1*, 540. (b) Wentworth, P.; Janda, K. D. *Chem. Commun.* **1999**, 1917. (c) Toy, P. H.; Janda, K. D. *Acc. Chem. Res.* **2000**, *33*, 546.
18. For recent examples of C_1-symmetric binaphthyl-based chiral catalysts, see: (a) Uozumi, Y.; Hayashi, T. *J. Am. Chem. Soc.* **1991**, *113*, 9887. (b) Uozumi, Y.; Lee, S.-Y.; Hayashi, T. *Tetrahedron Lett.* **1992**, *33*, 7185. (c) Hayashi, T.; Iwamura, H.; Naito, M.; Matsumoto, Y.; Uozumi, Y. *J. Am. Chem. Soc.* **1994**, *116*, 775. (d) Uozumi, Y.; Hayashi, T. *Tetrahedron Lett.* **1993**, *34*, 2335. (e) Sakai, N.; Mano, S.; Nozaki, K.; Takaya, H. *J. Am. Chem. Soc.* **1993**, *115*, 7033. (f) Horiuchi, T.; Ohta, T.; Nozaki, K.; Takaya, H. *Chem. Commun.* **1996**, 155. (g) Sakai, N.; Nozaki, K.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1994**, 395.
19. Tamai, Y.; Qian, P.; Matsunaga, K.; Miyano, S. *Bull. Chem. Soc. Jpn* **1992**, *65*, 817.
20. Kaiser, E.; Colescott, R. L.; Bossinger, C. D.; Cook, P. I. *Anal. Biochem.* **1970**, *34*, 595.